

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Peter W. Laird and Cindy A. Eads

Filing Date: April 2, 2001

Appl. No.: 09/825,566

5 For: EPIGENETIC SEQUENCES FOR ESOPHAGEAL ADENOCARCINOMA

Art Unit: 1634

Examiner: Jehan S. Sitton

Docket: 47675-18

Date: February 10, 2006

10

Mail Stop AF  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

15 **DECLARATION OF DR. PETER LAIRD UNDER 37 C.F.R. § 1.132**  
(IN SUPPORT OF RESPONSE UNDER 37 C.F.R. § 1.116)

Sir:

I, Dr. Peter William Laird, hereby declare:

20 1. I am an internationally recognized scientist and am presently employed as an Associate Professor, Department of Surgery, University of Southern California, Keck School of Medicine, Los Angeles, CA, and as an Associate Professor, Department of Biochemistry and Molecular Biology, University of Southern California, Keck School of Medicine, Los Angeles, CA. I received a B.S. degree in 1982 and an M.S. degree, *Cum Laude* in 1984, both from the  
25 University of Leiden, The Netherlands, and additionally received a Ph.D. degree from the University of Amsterdam, The Netherlands, in 1988.

2. I am an author or co-author of more than 64 peer-reviewed research articles and have been invited to present my research at numerous occasions (50) over that past 20 years, including at national and international meetings. My curriculum vitae is attached hereto as  
30 APPENDIX A.

3. In my capacity as a research professor and scientist, I am an expert on molecular biology, nucleic acid-based technologies and sequences and particularly on DNA methylation. Additionally, I am generally familiar with epigenetic sequences relating to esophageal adenocarcinoma. I am also familiar with bioinformatics databases, including, for example  
5 GenBank.

4. I am an original named inventor on the present patent application (09/825,566, and understand that the specification of the application has been objected to based on alleged introduction of 'new matter.' Specifically, I understand that the Examiner has alleged that the introduction, by applicants' agent, of SEQ ID NO:66 (MYOD gene sequence, corresponding to  
10 GenBank accession number AF027148 as listed in applicants' original specification at Table II) represents new matter in the absence of a statement that the SEQ ID NO:66 is the same as the sequence of GenBank accession number AF027148 at the time the invention was made, prior to the filing of the instant application or of the underlying provisional application.

5. I hereby declare that the MYOD sequence presently submitted as SEQ ID NO:66  
15 is the same as the MYOD sequence as it existed in GenBank at the time the invention was made, prior to the filing of the instant application or of the underlying provisional application. This conclusion is not only supported by my own records and analysis, but is also confirmed by the fact that the last update to the AF027148 sequence was on 07 AUG 1998 (see attached APPENDIX B, which is the current GenBank record for this sequence), and SEQ ID NO:66 is  
20 identical to that sequence.

6. I further declare that all statements made herein of my own knowledge are true and that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United  
25 States Code.

A handwritten signature in black ink, reading "Peter W. Laird". The signature is stylized with a large, looping "P" and a long horizontal stroke at the end.

Peter W. Laird

## APPENDIX A



### CURRICULUM VITAE *Current through February 9, 2006*

**Peter W. Laird, Ph.D.**

#### PERSONAL INFORMATION

|                         |   |
|-------------------------|---|
| <b>Name in Full</b>     | Peter William Laird, Ph.D.  |
| <b>Business Address</b> | USC/Norris Comprehensive Cancer Center<br>Room NOR 6418<br>1441 Eastlake Ave.<br>Los Angeles, CA 90089-9176 |
| <b>Business Phone</b>   | (323) 865-0650  |
| <b>Business Fax</b>     | (323) 865-0158  |
| <b>E-Mail Address</b>   | plaird@usc.edu  |
| <b>Home Address</b>     | 649 Forest Ave.<br>South Pasadena, CA 91030   |
| <b>Home Phone</b>       | (626) 403-7068  |
| <b>Place of Birth</b>   | Groton, Mass., USA  |
| <b>Citizenship</b>      | USA   |
| <b>Spouse</b>           | Ite Laird-Offringa, Ph.D.   |
| <b>Children</b>         | Two Daughters   |

#### EDUCATION

|           |   |
|-----------|---|
| 1978-1982 | University of Leiden, The Netherlands, B.Sc., 1982  |
| 1982-1984 | University of Leiden, The Netherlands, M.Sc., 1984  |
| 1984-1988 | University of Amsterdam, The Netherlands, Ph.D., 1988<br>with Dr. Piet Borst.<br>Ph.D. Thesis: "Trans Splicing in <i>Trypanosoma brucei</i> " |
| 1988-1991 | Postdoctoral Fellowship with Dr. Anton Berns<br>The Netherlands Cancer Institute, Amsterdam   |
| 1991-1996 | Postdoctoral Fellowship with Dr. Rudolf Jaenisch<br>The Whitehead Institute, MIT, Cambridge, MA   |

#### ACADEMIC APPOINTMENTS

|           |   |
|-----------|---|
| 1996-2002 | Assistant Professor, Department of Surgery, University of Southern California, School of Medicine, Los Angeles, CA. |
|-----------|---|

|              |   |
|--------------|---|
| 1996-2002    | Assistant Professor, Department of Biochemistry and Molecular Biology, University of Southern California, School of Medicine, Los Angeles, CA.      |
| 2002-Present | Associate Professor, Department of Surgery, University of Southern California, Keck School of Medicine, Los Angeles, CA.                            |
| 2002-Present | Associate Professor, Department of Biochemistry and Molecular Biology, University of Southern California, Keck School of Medicine, Los Angeles, CA. |

## **ADMINISTRATIVE POSITIONS**

|              |   |
|--------------|---|
| 1997-Present | Director of Basic Research, Department of Surgery                                 |
| 2004-Present | Co-Leader, Epigenetics and Regulation Program, Norris Comprehensive Cancer Center |

## **HONORS AND AWARDS**

|           |   |
|-----------|---|
| 1984      | M.Sc. degree <i>Cum Laude</i> from the University of Leiden     |
| 1984-1988 | ZWO (The Netherlands) Predoctoral Research Fellowship           |
| 1988-1991 | NWO (The Netherlands) Postdoctoral Research Fellowship          |
| 1991-1993 | National Research Service Award NIH/NCI Postdoctoral Fellowship |
| 1996      | Stop Cancer Lily Opas Research Career Development Award         |
| 1997      | New Investigator Award, USC Liver Disease Research Center       |

## **ADMINISTRATIVE ACTIVITIES**

### **University Committees**

|           |                            |
|-----------|----------------------------|
| 1996-1999 | Radiation Safety Committee |
|-----------|----------------------------|

### **School of Medicine Committees and Task Forces**

|              |  |
|--------------|--|
| 1997-1998    | Governance Document Task Force                                     |
| 1998         | School of Medicine Dean's "Kitchen Cabinet Task Force"             |
| 1998-2002    | School of Medicine Space Committee                                 |
| 2002-Present | Health Sciences Campus Interdepartmental Seminar Committee         |
| 2003-Present | Molecular Genetics and Cellular Biology Graduate Program Committee |
| 2003         | Member, Ad Hoc Committee for Promotion and Tenure                  |
| 2003         | Chair, Ad Hoc Committee for Promotion and Tenure                   |

### **Departmental Committees**

|           |   |
|-----------|---|
| 1997      | Norris Cancer Center Vivarium Renovation Planning Committee |
| 1997-1999 | Health Sciences Campus Basic Science Seminar Committee      |
| 1997      | Department of Surgery Web Page Development Committee        |

|              |  |
|--------------|--|
| 1997-Present | Director of Basic Research for the Department of Surgery   |
| 1998-Present | Surgical Council   |
| 1998         | Norris Cancer Center Faculty Recruitment Search Committee  |
| 2000         | Department of Preventive Medicine Molecular Epidemiology<br>Faculty Recruitment Search Committee |
| 2001         | Norris Cancer Center Scientific Review Committee   |
| 2001-2002    | Organization of Departmental Research Seminar Series for the<br>Department of Surgery            |
| 2001-2003    | Department of Biochemistry Ph.D. Admissions Committee  |
| 2003-Present | Department of Surgery Promotions and Appointments Committee                                      |
| 2003         | Department of Biochemistry Qualifying Exam Committee   |
| 2003         | Department of Biochemistry Faculty Merit Salary Increase<br>Evaluation Committee                 |

## PROFESSIONAL ACTIVITIES

|              |  |
|--------------|--|
| 1987         | Textbook Consultant and Reviewer, The Molecular Biology of the<br>Gene, 4th Edition; by J.D. Watson, N.H. Hopkins, J.W. Roberts,<br>J.A. Steitz, A.M. Weiner (1987); Benjamin/Cummings Publ. Co.<br>Inc., Menlo Park, Ca., USA |
| 1991-1992    | Whitehead Institute for Biomedical Research program (monthly<br>host) to inform high school teachers about current advances in<br>science  |
| 1992         | Organizing Committee, International Symposium "Molecular<br>Genetic Approaches to Mouse Development" in honor of Dr. Rudolf<br>Jaenisch's 50 <sup>th</sup> birthday  |
| 1992-1993    | Organizing Committee, Postdoc Night, Whitehead Institute for<br>Biomedical Research  |
| 1992-1994    | Organizing Committee, weekly seminar series at the Whitehead<br>Institute for Biomedical Research  |
| 1994         | Science Advisor to the Third Annual Ruffin Convocation on<br>"Genetics, Criminal Justice, and the Minority Community".<br>September 23-24, 1994, Northeastern University - College of<br>Criminal Justice                      |
| 1995-Present | Board of Directors, DNA Methylation Society  |
| 1996-Present | Full Member, USC/Norris Comprehensive Cancer Center  |
| 1996-1997    | Grant reviews for Southern California Environmental Health<br>Sciences Center  |
| 1997         | Co-founder, Orca Biosciences, Seattle, WA  |
| 1997-2000    | Grant reviews for Cancer Research Campaign, London, U.K.   |
| 1997-2002    | Study Section, Childrens Hospital Research Career Development<br>Awards (RCDA), Los Angeles, CA  |
| 1999         | Grant review, Alberta Cancer Board   |
| 2000-Present | Consultant, Epigenomics, A.G.  |
| 2001-Present | Scientific Advisory Board, Epigenomics, A.G.   |

|              |  |
|--------------|--|
| 2002-Present | American Cancer Society Internal Grant Review  |
| 2004         | Co-Chair and Organizer, FASEB Meeting on Biological Methylation, July 10-15, 2004, Saxtons River, Vermont  |
| 2004         | Steering Committee, Entertainment Industry Foundation, Breast Cancer Biomarker Project   |
| 2004-Present | Editorial Board, Cancer Biology & Therapy  |
| 2004-Present | Scientific Advisory Board, Canary Fund   |
| 2005         | Wright Foundation Ad Hoc Grant Review  |
| 2005         | Member of the 2005-2006 Selection Committee for the Kirk A. Landon-AACR Prize for Basic Cancer Research for the American Association of Cancer Research (AACR) |
| 2006         | NIH Study Section Epidemiology C (EPIC) Members Study Section  |

## TEACHING ACTIVITIES

|              |  |
|--------------|--|
| 1996         | Lecturer, Surgical Residency Core Curriculum.  |
| 1997         | Lecturer and paper advisor, Special Topics: Frontiers in Basic and Applied Sciences, PATH 599, University of Southern California.                                  |
| 1997-2003    | Department of Biochemistry Ph.D. Qualifying exam question design and grading.  |
| 1998-Present | Lecturer, exam question design and grading, Human Biology System, Medical School First Year Curriculum. (Currently: Core Curriculum, Cell Structure and Function). |
| 1998-2004    | Lecturer, exam question design and grading, and paper advisor, Molecular Genetics, INTD 561, University of Southern California.                                    |
| 1998-Present | Lecturer, exam question design and grading, Development and Cancer, BIOC 542, University of Southern California.   |
| 1998-2002    | Lecturer, exam question design and grading, Human Molecular Genetics, BIOC 543, University of Southern California.   |
| 1998-2002    | Lecturer, exam question design and grading, Molecular Biology of Cancer, INTD 504, University of Southern California.  |
| 1999-Present | Lecturer, Genetic Epidemiology, PM 533, University of Southern California.   |
| 2004-Present | Organizer Epigenetics Module, Lecturer, exam question design and grading, Molecular Biology of Cancer, INTD 504, University of Southern California.                |

## TRAINEES

### M.S.

|           |               |
|-----------|---------------|
| 1997-1999 | Ruby Chan     |
| 1997-2001 | René Malekian |

2002-2004 Cindy Lin

**Ph.D.**

|              |                  |
|--------------|------------------|
| 1996-2001    | Matilda Chan     |
| 1997-2000    | Cindy Eads       |
| 1998-2002    | Binh Trinh       |
| 2000-2005    | Nicole Sodir     |
| 2000-Present | Myungjin Kim     |
| 2001-Present | Sahar Houshdaran |
| 2001-Present | Kwangho Lee      |
| 2003-Present | Toshinori Hinoue |
| 2003-Present | Shirley Oghamian |

**Postdoctoral**

|              |                     |
|--------------|---------------------|
| 1996-1998    | Zhenggang Xiong     |
| 1999-2000    | Saj Wajed           |
| 2000-2001    | Karen Uhlmann       |
| 2003-2004    | Gyeong Hoon Kang    |
| 2003-2004    | Tasha Gandamihardja |
| 2004-2005    | Binh Trinh          |
| 2002-Present | Mihaela Campan      |
| 2003-Present | Daniel Weisenberger |
| 2005-Present | Nicole Sodir        |

**OVERVIEW OF RESEARCH ACTIVITY**

Our goal is to contribute to a detailed understanding of the molecular basis of cancer, which in turn may lead to improved treatment strategies, earlier detection methods, and more accurate diagnoses. Our main focus is to understand the role of DNA methylation in cancer. DNA methylation occurs in mammals as a normal, enzymatic modification of cytosine bases and is associated with gene silencing. We take a multi-disciplinary approach to understanding how DNA methylation affects the cancer process. Research methods employ a combination of molecular biology, cell culture, genetically manipulated mice, as well as population-based epidemiologic approaches in humans, and collaborative clinical studies. Our research spans from studies of the most basic cellular mechanisms to devising new diagnostic methods for clinicians. We have close interactions with other molecular biologists, biochemists, epidemiologists, statisticians, pathologists, surgeons, and oncologists. In recent years we have demonstrated the complete genetic suppression of tumor formation by reduced DNA methylation in a mouse model of the human disease Familial Adenomatous Polyposis, and we have developed several novel DNA methylation analysis techniques, including COBRA and a patented high-throughput technique called "MethyLight".

**INVITED LECTURES**

- 10/24/1985 SFB 165 Symposium "RNA Synthesis and Processing", Würzburg, Germany. *Speaker*: "Discontinuous Synthesis of mRNAs in Trypanosomes"
- 08/26/1986 17th FEBS Meeting, Berlin, Germany. *Speaker*: "Discontinuous Synthesis of mRNAs in Trypanosomes".
- 12/17/1986 University of Geneva, Dept. of Molecular Biology, Geneva, Switzerland. *Invited Seminar*: "Discontinuous Synthesis of mRNAs in Trypanosomes".
- 12/18/1986 University of Bern, Institute of General Microbiology, Bern, Switzerland. *Invited Seminar*: "Transsplicing in *Trypanosoma brucei*".
- 05/23/1989 University of Edinburgh, U.K. *Invited Seminar*: "The Mouse Pim-1 Proto-Oncogene".
- 10/26/1990 Topics in Biotechnology, Symposium at International Institute of Cellular and Molecular Pathology, University of Brussels, Belgium. *Speaker*: "Transsplicing in *Trypanosoma brucei*".
- 09/01/1990 The 1990 Cold Spring Harbor Symposium on Mouse Molecular Genetics., Cold Spring Harbor, New York, NY. *Speaker*: "Gene Targeting of the Murine Pim-1 Proto-oncogene".
- 09/04/1994 The 1994 Cold Spring Harbor Symposium on Mouse Molecular Genetics., Cold Spring Harbor, New York. *Speaker*: "Mutagenicity of DNA Methyltransferase in Mammalian Cells".
- 02/14/1995 Netherlands Cancer Institute, Amsterdam, The Netherlands. *Invited Seminar*: "The Role of DNA Methylation in Cancer".
- 11/09/1996 153<sup>rd</sup> Meeting of The Society of Clinical Surgery, Los Angeles, CA. *Speaker*: "Gene Targeting in Cancer Research".
- 11/10/1996 American Association for the Study of Liver Disease, 47<sup>th</sup> Annual Meeting, Chicago, IL. *Speaker*: "The Use of Gene Targeting to Study the Role of DNA Methylation in Cancer".
- 12/12/1996 Childrens Hospital Los Angeles, Los Angeles, CA. *Invited Seminar*: "The Role of DNA Methylation in Cancer".
- 06/16/1997 FASEB Summer Research Conference on Biological Methylation. Saxtons River, Vermont. *Chair*: "DNA Methylation: Gene Expression & Cancer".
- 09/01/1997 Symposium: Barrett's Ablation Therapy, Chateau de la Bretesche, Brittany, France. *Speaker*: "Studies on the Trigger for Barrett's Metaplasia Using Knock-Out Mice and Rats".
- 09/05/1997 4<sup>th</sup> New England Biolabs Workshop on Biological DNA Modification. Innsbrück – Igls, Austria. *Speaker*: "Comparison of DNA Methylation Patterns of Matched Mismatch Repair Proficient and Deficient Human Colorectal Tumors using COBRA". *Chair*: "Genetic Imprinting and Epigenetics".
- 03/03/1998 Society of Toxicology, 37<sup>th</sup> Annual Meeting. Seattle, WA. *Speaker*: "Altered DNA Methylation, Epigenetics and Cancer".
- 08/10/1998 Gordon Research Conference on DNA Alterations in Transformed Cells. Colby-Sawyer College, NH. *Speaker*: "DNA Methylation as a Key Player in Genetic and Epigenetic Mechanisms of Cancer".
- 09/25/1998 Curie Workshop on Epigenetics and DNA Methylation. Paris, France. *Speaker*: "The Role of DNA Methylation in Colorectal Tumorigenesis".
- 03/30/1999 Arizona Cancer Center, Tucson, AZ. *Invited Seminar*: "The Role of DNA Methylation in Cancer".

- 05/18/1999 University of California Santa Barbara. Santa Barbara, CA. *Invited Seminar*: "The Role of DNA Methylation in Cancer".
- 07/19/1999 FASEB Summer Research Conference on Biological Methylation. Saxtons River, Vermont. *Speaker*: "High-Throughput Analysis of DNA Methylation and DNA Methyltransferase Expression in Human Tumors".
- 04/02/2000 91<sup>st</sup> Annual AACR Meeting. San Francisco, CA. *Chair*: "DNA Methylation I"
- 09/13/2000 National Cancer Institute Colorectal Family Registry Meeting. Toronto, CA. *Speaker*: "High-Throughput Studies of DNA Methylation with Paraffin-Embedded Tissue".
- 10/27/2000 Modeling Human Colo-Rectal Cancer in Mice. The Jackson Laboratory, Bar Harbor, ME. *Speaker*: "Complete Genetic Suppression of Gastro-Intestinal Tumorigenesis by *Dnmt1* Hypomorphic Alleles".
- 02/26/2001 Medical and Surgical Aspects of Esophageal and Foregut Disorders: Pathophysiology and Treatment. Mauna Kea Beach Hotel, Hawaii. *Speaker*: "Molecular Markers of Adenocarcinoma".
- 04/30/2001 Vanderbilt University Medical Center. Nashville, TN. *Invited Seminar*: "Clinical and Biological Implications of DNA Methylation Changes in Cancer".
- 07/21/2001 FASEB Summer Research Conference on Biological Methylation. Saxtons River, Vermont. *Speaker*: "High-Throughput Analysis of DNA Methylation and DNA Methyltransferase Expression in Human Tumors".
- 08/06/2001 Trans-HHS Workshop: Diet, DNA Methylation Processes and Health. Bethesda, MD. *Speaker and Session Chair*: "Current Methodologies in DNA Methylation Analysis".
- 09/19/2001 AACR Special Conference "Epigenetics of Cancer". Palm Desert, CA. *Speaker*: "Clinical and Biological Implications of DNA Methylation Changes in Cancer".
- 11/03/2001 Association of Pathology Chairs and Managers Western and Mid-Western Annual Conference. Puerto Vallarta, Mexico. *Speaker*: "Molecular Diagnostics Using Genomic DNA Methylation Patterns".
- 12/03/2001 NCI Workshop "Epigenetics in Early Cancer Detection and Risk Assessment". Bethesda, MD. *Speaker*: Technology Advancement in Epigenetics and Cancer.
- 05/29/2002 CNIO Cancer Conference on "DNA Methylation and Chromatin". Madrid, Spain. *Speaker*: "DNA Methylation and Mismatch Repair".
- 08/07/2002 FASEB Summer Research Conference on Folic Acid, Vitamin B12, and One-Carbon Metabolism. Saxtons River, Vermont. *Speaker*: "DNA Methylation: An Alternative Pathway to Cancer".
- 09/26/2002 European Surgical Institute Symposium "US Meets Europe on Barrett's". Norderstedt, Germany. *Speaker*: "Epigenetic Alterations and Progression to Adenocarcinoma".
- 01/31/2003 Seventh EDRN Steering Committee Meeting. Birmingham, Alabama. *Speaker and Panelist*: "Planning for Methylation Validation Studies Across Cancer Sites: Principle, Practice and Implementation".
- 08/17/2003 Gordon Research Conference on New Frontiers in Cancer Detection and Diagnosis, Andover, New Hampshire. *Speaker*: "DNA Methylation Profiles in Breast Cancer".
- 08/22/2003 Fred Hutchinson Cancer Research Center. Seattle, Washington. *Invited Seminar*: "DNA Methylation and Cancer".

- 09/11/2003 Southern California Environmental Health Sciences Center Annual Retreat. Los Angeles, California. *Speaker: "Environmental Epigenomics"*.
- 02/28/2004 Canadian Digestive Disease Week. Banff, Canada. *Speaker: "Epigenetic Alterations in Colorectal Cancer"*.
- 05/14/2004 Weissenburg Symposium on DNA Methylation - an Important Genetic Signal. Cologne, Germany, 2004. *Speaker: "DNA Methylation and Cancer: Of Mice and Men"*.
- 05/19/2004 Epigenetics Think Tank, National Cancer Institute, Bethesda, Maryland. *Invited Panel Member*.
- 10/16/2004 Third Annual AACR International Conference "Frontiers in Cancer Prevention Research". Seattle, Washington. *Speaker: "DNA Methylation, Carcinogenesis and Cancer Prevention"*.
- 11/12/2004 AACR Special Conference "Chromatin, Chromosomes and Cancer Epigenetics". Waikoloa, Hawaii. *Speaker: "Exploring the Validity of the CpG Island Methylator Phenotype in Colorectal Cancer by MethyLight"*.
- 02/07/2005 Fred Hutchinson Cancer Research Center, Seattle, WA. *Invited Seminar: "CpG Island Methylator Phenotype in Colorectal Cancer – Resolving the Controversy"*.
- 02/23/2005 NCI Science Writer's Workshop, Los Angeles, CA. *Speaker: "DNA-based early detection of cancer"*.
- 04/05/2005 American Society of Pharmacology and Experimental Therapeutics (ASPET) Annual Meeting, San Diego, CA. *Speaker: "The Promise of DNA Methylation Markers in Cancer Prognostication"*.
- 05/25/2005 Canary Fund Symposium "Early Detection of Cancer: Realizing the Promise", Stanford University, Palo Alto, CA. *Speaker and Panel Chair: "DNA-Based Markers"*.
- 06/15/2005 AACR Human Epigenome Workshop "Toward a Human Epigenome Project", Landsdowne, VA. *Speaker: "Disease States"*.
- 11/28/2005 NCI Workshop "Defining the Cancer Epigenome", Rockville, MD. *Speaker and Panel Chair: "Epigenome Technology"*.
- 11/30/2005 NCI Workshop "Translational Epigenetic Science in Cancer", Rockville, MD. *Speaker: "Diagnosis"*

## **PATENTS**

- Issued U.S. Patent # 6,331,393

Process for High Throughput Assay To Measure DNA Methylation.

Inventors: Peter W. Laird, Cindy A. Eads and Kathleen D. Danenberg.

Date Filed: 14 May 1999.

Date of Issue: December 18, 2001

- U.S. Patent Application Serial Number 06/193,839.

Epigenetic Sequences for Esophageal Adenocarcinoma.

Inventors: Peter W. Laird and Cindy A. Eads.

Date Filed: April 2, 2000

Status: Decision Pending

- U.S. Patent Application.

A New Assay for the Detection and Quantitation of Hemimethylation. Inventors: Peter A. Jones, Gangning Liang, Yoshitaka Tomigahara and Peter W. Laird.

Date Filed: November 9, 2000.

Status: Decision Pending

- U.S. Patent Application.

Association of Breast Cancer DNA Methylation Profiles with Hormone Receptor Status and Response to Tamoxifen. Inventors: Martin Widschwendter, Kim Siegmund, Peter A. Jones and Peter W. Laird.

Date Filed: June 1, 2004.

Status: Decision Pending

## **PAST RESEARCH FUNDING**

|           |  |
|-----------|--|
| 1991-1993 | NIH / NCI 1F32CA009097-01.<br>In Vivo Analysis of the Wilms' Tumor Suppressor Gene.<br>Principal Investigator: Peter Laird.<br>NRSA Postdoctoral Fellowship; Sponsor: Dr. Rudolf Jaenisch<br>\$ 84,600 direct costs. |
| 1996-1997 | NIH / NCI Cancer Center Core Grant Pilot, 2CA-14089-21.<br>The Role of DNA Methylation in Gastrointestinal Cancer.<br>Principal Investigator: Peter Laird.<br>\$ 20,000 direct costs.                                |
| 1997-1998 | USC Liver Disease Research Center Pilot Grant.<br>DNA Methylation and Chromosomal Stability in Intestinal Neoplasia.<br>Principal Investigator: Peter Laird.<br>\$ 16,483 direct costs.                              |
| 1998      | NIH PAR-95-082.<br>Improvement of Animal Resources at the Norris Cancer Center.<br>Co-investigator. Principal Investigator: Dr. Rob Maxson.<br>\$ 618,096 direct costs for Norris (no Laird lab component).          |
| 1996-1999 | Stop Cancer Career Development Award.<br>\$ 300,000 direct costs from Stop Cancer and Norris Cancer Center.  |
| 1997-1999 | NIH / NCI / SEER N01 PC067010.<br>Hormone Replacement Therapy and Colon Cancer.<br>Co-Investigator. Principal Investigator: Dr. Ron Ross.<br>\$ 164,482 direct costs for Laird lab component.                        |

|           |   |
|-----------|---|
| 1998-2001 | <p>ACS RPG-98-214-01-CCE.<br/> The Role of DNA Methylation in Esophageal Adenocarcinoma.<br/> Co-investigator. Principal Investigator: Dr. Kristin Skinner.<br/> \$ 11,472 direct costs for Laird lab component.</p>    |
| 1997-2002 | <p>NIH / NCI, 1 R01 CA75090-01.<br/> Suppression of Intestinal Neoplasia by DNA Hypomethylation.<br/> Principal Investigator: Peter Laird<br/> \$ 688,067 direct costs.</p>   |
| 2001-2002 | <p>The Wright Foundation.<br/> Pilot Cancer Epigenome Project.<br/> Principal Investigator: Peter Laird<br/> \$ 49,902 direct costs.</p>  |
| 2002-2003 | <p>NIH / NCI Contractual Agreement, 263-MQ-113043-1<br/> DNA Methylation in Adenomatous Polyps.<br/> Principal Investigator: Peter Laird<br/> \$ 56,000 direct costs.</p>   |
| 2002-2003 | <p>Innovative Cancer Control Initiative Pilot Project<br/> Development of Novel Serum Markers for the Early Detection<br/> of Prostate Cancer<br/> Principal Investigator: Peter Laird<br/> \$ 24,425 direct costs.</p> |
| 2003      | <p>Fidelity Foundation<br/> Epigenetic Regulation and Brain Disease<br/> Co-investigator. Principal Investigator: Dr. Rudolf Jaenisch<br/> \$ 75,000 direct costs for Laird lab component.</p>                          |
| 2003      | <p>Contract with Epigenomics, A.G.<br/> DNA Methylation Analysis of Breast Cancer<br/> Principal Investigator: Peter Laird<br/> \$ 53,750 direct costs.</p>   |
| 1999-2004 | <p>NIH / NCI, 2 P01 CA17054-22<br/> Iatrogenic Causes of Cancer.<br/> Co-investigator. Principal Investigator: Dr. Ron Ross.<br/> \$183,944 direct costs for Laird lab component.</p>                                   |
| 2000-2004 | <p>NIH / NCI, 1 R01 CA77376-01.<br/> DNA Methylation and Colorectal Polyps.<br/> Co-investigator. Principal Investigator: Dr. Robert Haile.<br/> \$ 1,088,482 direct costs for Laird lab component.</p>                 |

|           |  |
|-----------|--|
| 2000-2004 | NIH / NCI, 1 R01 CA84339-01.<br>Detection of Occult Metastases in Lung Cancer Patients.<br>Co-investigator. Principal Investigator: Dr. Richard Cote.<br>\$ 40,796 direct costs for Laird lab component.     |
| 2002-2005 | NIH / NIEHS 1 R21 ES11672-01<br>Environmental Epigenomics<br>Principal Investigator: Peter Laird<br>\$ 450,000 direct costs.   |
| 2003-2005 | NIH / NCI 1 R21 CA102247-01<br>Lung Cancer Diagnosis Using DNA Methylation Signatures<br>Co-investigator. Principal Investigator: Dr. Ite Laird-Offringa.<br>\$ 65,000 direct costs for Laird lab component. |

## **ACTIVE RESEARCH FUNDING**

|           |   |
|-----------|---|
| 2002-2006 | NIH / NCI 1 RO1 CA097346-01<br>Statistical Models in Epigenomics<br>Co-investigator. Principal Investigator: Dr. Kimberly Siegmund<br>\$ 27,625 direct costs for Laird lab component. |
| 2002-2007 | NIH / NCI U01 CA074799<br>Colorectal Cancer Family Registry<br>Co-investigator. Principal Investigator: Dr. Robert Haile<br>\$ 321,236 direct costs for Laird lab component.          |
| 2002-2007 | NIH / NCI 1 R01 CA096958-01<br>DNA Methylation Markers in Ovarian Cancer<br>Principal Investigator: Peter Laird<br>\$ 1,001,250 direct costs.   |
| 2002-2007 | NIH / NCI, 1 R01 CA001815-01.<br>DNA Methylation Markers in Esophageal Adenocarcinoma.<br>Principal Investigator: Peter Laird<br>\$ 1,125,000 direct costs.                           |
| 2003-2007 | NIH / NCI, 2 R01 CA75090-5A1.<br>Suppression of Intestinal Neoplasia by DNA Hypomethylation.<br>Principal Investigator: Peter Laird<br>\$ 1,125,000 direct costs.                     |
| 2005-2010 | NIH / NCI, 1 R01 CA111187-1A1<br>HIV Associated DNA Hypermethylation in Cervical Cancer<br>Principal Investigator: Kiviat, (PI) (Subcontract from U of Washington)                    |

\$ 224,980 direct costs for Laird lab component.

## PUBLICATIONS

1. **Laird, P.W.**, Kooter, J.M., Loosbroek, N. and Borst, P.  
Mature mRNAs of *Trypanosoma brucei* Possess a 5' Cap Acquired by Discontinuous RNA Synthesis.  
**Nucleic Acids Research** 13, 4253-4266, 1985.
2. **Laird, P.W.**, Zomerdiik, J.C.B.M., de Korte, D. and Borst, P.  
*In Vivo* Labelling of Intermediates in the Discontinuous Synthesis of mRNAs in *Trypanosoma brucei*.  
**EMBO Journal** 6, 1055-1062, 1987.
3. Gibson, W.C., White, T.C., **Laird, P.W.** and Borst, P.  
Stable Introduction of Exogenous DNA into *Trypanosoma brucei*.  
**EMBO Journal** 6, 2457-2461, 1987.
4. Imboden, M.A., **Laird, P.W.**, Affolter, M. and Seebeck, T.  
Transcription of the Intergenic Regions of the Tubulin Gene Cluster of *Trypanosoma brucei*: Evidence for a Polycistronic Transcription Unit in a Eukaryote.  
**Nucleic Acids Research** 15, 7357-7368, 1987.
5. **Laird, P.W.**, ten Asbroek, A.L.M.A. and Borst, P.  
Controlled Turnover and 3' Trimming of the Trans Splicing Precursor of *Trypanosoma brucei*.  
**Nucleic Acids Research** 15, 10087-10103, 1987.
6. **Laird, P.W.**  
Trans Splicing in Trypanosomes - Archaism or Adaptation?  
**Trends in Genetics** 5, 204-208, 1989.
7. **Laird, P. W.**, Zijderfeld, A., Linders, K., Rudnicki, M.A., Jaenisch, R. and Berns, A.  
Simplified Mammalian DNA Isolation Procedure.  
**Nucleic Acids Research** 19, 4293, 1991.
8. van der Lugt, N.M.T., Robanus Maandag, E., te Riele, H., **Laird, P.W.** and Berns, A.  
A pgk::hprt Fusion as a Selectable Marker for Targeting of Genes in Mouse Embryonic Stem Cells: Disruption of the T-cell Receptor  $\beta$ -Chain-Encoding Gene.  
**Gene** 105, 263-267, 1991.
9. **Laird, P.W.**, van der Lugt, N.M.T., Clarke, A.R., Domen, J., Linders, K., McWhir, J., Berns, A. and Hooper, M.  
*In Vivo* Analysis of *Pim-1* Deficiency.  
**Nucleic Acids Research** 21, 4750-4755, 1993.

10. Domen, J., van der Lugt, N.M.T., **Laird, P.W.**, Saris, C.J.M., Clarke, A., Hooper, M. and Berns, A.  
Impaired IL-3 Response in *Pim-1* Deficient Bone Marrow Derived Mast Cells.  
**Blood** 82, 445-4452, 1993.
11. Domen, J., van der Lugt, N.M.T., Acton, D., **Laird, P.W.**, Linders, K. and Berns, A.  
Pim-1 Levels Determine the Size of Early B Lymphoid Compartments in Bone Marrow.  
**Journal of Experimental Medicine** 178, 1665-1673, 1993.
12. Domen, J., van der Lugt, N.M.T., **Laird, P.W.**, Saris, C.J.M., Berns, A.  
Analysis of *Pim-1* Function in Mutant Mice.  
**Leukemia**, 7(suppl 2), S108-S112, 1993.
13. **Laird, P.W.**, Jaenisch, R.  
DNA Methylation and Cancer.  
**Human Molecular Genetics**, 3, 1487-1495, 1994.
14. Berns, A., van der Lugt, N.M.T., Alkema, M., van Loohuizen, M., Domen, J., **Laird, P.W.**, Jonkers, J.  
Mouse Model Systems to Study Multistep Tumorigenesis.  
**Cold Spring Harbor Symposia Quantitative Biology**, 59, 435-447, 1994.
15. **Laird, P.W.**, Jackson-Grusby, L., Fazeli, A., Dickinson, S.L., Jung, W.E., Li, E., Weinberg, R.A. and Jaenisch, R.  
Suppression of Intestinal Neoplasia by DNA Hypomethylation.  
**Cell** 81, 197-205, 1995.
16. Johnson, K.A., Lerner, C.P., DiLacio, L.C., **Laird, P.W.**, Sharpe, A.H. and Simpson, E. M.  
Transgenic Mice for the Preparation of Hygromycin-Resistant Primary Embryonic Fibroblast Feeder Layers for Embryonic Stem Cell Selections.  
**Nucleic Acids Research** 23, 1273-1275, 1995.
17. Tucker, K.L., Beard, C., Dausman, J., Jackson-Grusby, L., **Laird, P.W.**, Lei, H., Li, E. and Jaenisch, R.  
Germ-line Passage is Required for Establishment of Methylation and Expression Patterns of Imprinted but not of Nonimprinted Genes  
**Genes and Development** 10, 1008-1020, 1996.
18. **Laird, P.W.**, Jaenisch, R.  
The Role of DNA Methylation in Cancer Genetics and Epigenetics.  
**Annual Review of Genetics**, 30, 441-464, 1996.
19. Jackson-Grusby, L., **Laird, P.W.**, Magge, S.N., Moeller, B.J. and Jaenisch, R.  
Mutagenicity of 5-aza-2'-deoxycytidine is Mediated by DNA Methyltransferase.

**Proceedings of the National Academy of Sciences U. S. A.** 94, 4681-4685, 1997.

20. **Laird, P.W.**  
Oncogenic Mechanisms Mediated by DNA Methylation.  
**Molecular Medicine Today** 3, 223-229, 1997.
21. Xiong, Z. and **Laird, P.W.**  
COBRA - A Sensitive and Quantitative DNA Methylation Assay.  
**Nucleic Acids Research** 25, 2532-2534, 1997.
22. Jones, P.A. and **Laird, P.W.**  
Cancer Epigenetics Comes of Age.  
**Nature Genetics** 21, 163-167, 1999.
23. Fein, M., Peters, J.H., Baril, N., McGarvey, M., Chandrasoma, P., Shibata, D., **Laird, P.W.**, and Skinner, K.A.  
Loss of Function of Trp53, but not Apc, Leads to the Development of Adenocarcinoma in Mice with Jejunoesophageal Reflux.  
**J. Surgical Research** 83, 48-55, 1999.
24. Eads, C.A., Danenberg, K.D., Kawakami, K., Saltz, L.B., Danenberg, P.V. and **Laird, P.W.**  
CpG Island Hypermethylation in Human Colorectal Tumors is not Associated with DNA Methyltransferase Overexpression.  
**Cancer Research** 59, 2302-2306, 1999.
25. Fein, M., Fuchs, K.H., Peters, J.H., Chandrosoma, P., Shibata, D., **Laird, P.W.**, Skinner, K.A.  
Reflux of Duodenal Juice Induces Esophageal Carcinoma in Trp53-Knockout Mice.  
**Langenbecks Archives of Surgery Suppl**, 1, 99-103, 1999.
26. Pao, M.M., Liang, G., Xiong, Z., Schmutte, C., Tsai, Y.C., **Laird, P.W.** and Jones, P.A.  
DNA Methylator and Mismatch Repair Phenotypes are Not Mutually Exclusive in Colorectal Cancer Cell Lines.  
**Oncogene** 19, 943-952, 2000.
27. Eads, C.A., Danenberg, K.D., Kawakami, K., Saltz, L.B., Blake, C., Shibata, D., Danenberg, P.V., and **Laird, P.W.**  
MethyLight: a high-throughput assay to measure DNA methylation.  
**Nucleic Acids Research** 28, e32 i-viii, 2000.
28. Eads, C.A., Lord, R.V, Kurumboor, S.K., Wickramasinghe, K., Skinner, M.L., Long, T.I., Peters, J.H., DeMeester, T.R., Danenberg, K.D., Danenberg, P.V., **Laird, P.W.**, and Skinner, K.A. Fields of Aberrant CpG Island Hypermethylation in Barrett's Esophagus and Associated Adenocarcinoma.  
**Cancer Research** 60, 5021-5026, 2000.

29. Kawakami, K., Brabender, J., Lord, R.V., Groshen, S., Greenwald, B.D., Krasna, M.J., Yin, J., Fleisher, A.S., Abraham, J.M., Beer, D.G., Sidransky, D., Huss, H.T., Demeester, T.R., Eads, C., **Laird, P.W.**, Ilson, D.H., Kelsen, D.P., Harpole, D., Moore, M.B., Danenberg, K.D., Danenberg, P.V., and Meltzer, S.J.  
Hypermethylated APC DNA in Plasma and Prognosis of Patients with Esophageal Adenocarcinoma.  
**J. Natl. Cancer Institute** 92, 1805-1811, 2000.
30. Eads, C.A., Lord, R.V, Wickramasinghe, K., Long, T.I., Kurumboor, S.K., Bernstein, L., Peters, J.H., DeMeester, S.R., DeMeester, T.R., Skinner, K.A., and **Laird, P.W.**  
Epigenetic Patterns in the Progression of Esophageal Adenocarcinoma.  
**Cancer Research** 61, 3410-3418, 2001.
31. Wajed, S., **Laird, P.W.**, and DeMeester, T.R..  
DNA Methylation - An Alternative Pathway to Cancer?  
**Annals of Surgery** 234, 10-20, 2001.
32. Xiong, Z., Wu, A.H., Bender, C.M., Tsao, J.L., Blake, C., Shibata, D., Jones, P.A., Yu, M.C., Ross, R.K., and **Laird, P.W.**  
Mismatch Repair Deficiency and CpG Island Hypermethylation in Sporadic Colon Adenocarcinomas.  
**Cancer Epidemiology, Biomarkers & Prevention** 10, 799-803, 2001.
33. Markl, I.D.C., Cheng, J., Liang, G., Shibata, D., **Laird, P.W.**, and Jones, P.A.  
Global and Gene-Specific Epigenetic Patterns in Human Bladder Cancer Genomes are Relatively Stable In Vivo and In Vitro over Time.  
**Cancer Research** 61, 5875-5884, 2001.
34. Chan, M.F., van Amerongen, R., Nijjar, T., Cuppen, E., Jones, P.A., and **Laird, P.W.**  
Reduced Rates of Gene Loss, Gene Silencing, and Gene Mutation in Dnmt1-Deficient ES Cells.  
**Molecular and Cellular Biology** 21, 7587-7600, 2001.
35. Trinh, B.N., Long, T.I., and **Laird, P.W.**  
DNA Methylation Analysis by MethyLight Technology.  
**Methods** 25, 456-462, 2001.
36. Eads, C.A. and **Laird, P.W.**  
COBRA: Combined Bisulfite Restriction Analysis.  
**Methods in Molecular Biology** 200, 71-85, 2002.
37. Liang, G., Chan, M.F., Tomigahara, Y., Tsai, Y.C., Gonzales, F.A., Li, E., **Laird, P.W.**, and Jones, P.A.  
Cooperativity between DNA Methyltransferases in the Maintenance Methylation of Repetitive Elements.

**Molecular and Cellular Biology** 22, 480-491, 2002.

38. Müller-Ehmsen, J., Whittaker, P., Kloner, R.A., Dow, J.S., Sakoda, T., Long, T.I., **Laird, P.W.**, and Kedes, L.H.  
Survival and Development of Neonatal Rat Cardiomyocytes Transplanted into Adult Myocardium.  
**Journal of Molecular and Cellular Cardiology** 34, 107-116, 2002.
39. Eads, C.A., Nickel, A.E., and **Laird, P.W.**  
Complete Genetic Suppression of Polyp Formation and Reduction in CpG-Island Hypermethylation in *ApcMin/+*, *Dnmt1*-Hypomorphic Mice.  
**Cancer Research** 62, 1296-1299, 2002.
40. Virmani, A. K., Tsou, J.A., Siegmund, K.D., Shen, L., Long, T.I., **Laird, P.W.**, Gazdar, A.F., and Laird-Offringa, I.A.  
Hierarchical Clustering of Lung Cancer Cell Lines Using DNA Methylation Markers.  
**Cancer Epidemiology, Biomarkers and Prevention** 11, 291-297, 2002.
41. Trinh, B.N., Long, T.I., Nickel, A.E., Shibata, D., and **Laird, P.W.**  
DNA Methyltransferase Deficiency Modifies Cancer Susceptibility in Mice Lacking DNA Mismatch Repair  
**Molecular and Cellular Biology** 22, 2906-2917, 2002.
42. Müller-Ehmsen, J., Peterson, K.L., Kedes, L. Whittaker, P., Dow, J.S., Long, T.I., **Laird, P.W.**, and Kloner, R.A.  
Rebuilding a Damaged Heart: Long-Term Survival of Transplanted Neonatal Rat Cardiomyocytes after Myocardial Infarction and Effect on Cardiac Function.  
**Circulation** 105, 1720-1726, 2002.
43. Siegmund, K.D. and **Laird, P.W.**  
Analysis of Complex Methylation Data.  
**Methods** 27, 170-178, 2002.
44. Trinh, B.N., Ong, C.N., Coetzee, G.A., Yu, M.C., and **Laird, P.W.**  
Thymidylate Synthase: A Novel Genetic Determinant of Plasma Homocysteine and Folate Levels.  
**Human Genetics** 111, 299-302, 2002.
45. Ehrlich, M., Jiang, G., Dome, J.S., Yu, M., Long, T.I., Widshwendter, M., Tomlinson, G.E., Chintagumpala, M., Champagne, M., Parham, D.M., Liang, G., Youn, B., Sohn, O.S., and **Laird, P.W.**  
Hypomethylation and Hypermethylation of DNA in Wilms Tumors  
**Oncogene** 21, 6694-6702, 2002.
46. Tsao, J.L., Dudley, S., Kwok, B., Nickel, A.E., **Laird, P.W.**, Siegmund, K.D., Liskay, R.M., and Shibata, D.

Diet, Cancer and Aging in DNA Mismatch Repair Deficient Mice.  
**Carcinogenesis** 23, 1807-1810, 2002.

47. Tsien, F., Fiala, E.S., Youn, B., Long, T.I., **Laird, P.W.**, Weissbecker, K., and Ehrlich, M.  
Prolonged Culture of Normal Chorionic Villus Cells Yields ICF Syndrome-Like Chromatin Decondensation and Rearrangements.  
**Cytogenetics and Genome Research** 98, 13-21, 2002.
48. Aparicio, A., Eads, C.A., Leong, L., **Laird, P.W.**, Newman, N., Synold, T., Baker, S., Zhou, M., Weber, J.  
Phase I Trial of Continuous Infusion 5-Aza-2'-Deoxycytidine.  
**Cancer Chemotherapy and Pharmacology** 51, 231-239, 2003.
49. **Laird, P.W.**  
The Power and the Promise of DNA Methylation Markers  
**Nature Reviews Cancer** 3, 253-266, 2003.
50. Uhlmann, K., Rohde, K., Zeller, C., Szymas, J., Vogel, S., Marczinek, K., Thiel, G., Nürnberg, P., **Laird, P.W.**  
Glioma Subtypes Show Characteristic Patterns of DNA Hypomethylation and Hypermethylation.  
**International Journal of Cancer** 106, 52-59, 2003.
51. Pagliarulo, V., George, B., Beil, S.J., Groshen, S., **Laird, P.W.**, Cai, J., Willey, J., Cote, R.J., Datar, R.H.  
Sensitivity and Reproducibility of Standardized Competitive RT PCR for Transcript Quantification and its Comparison with Real-Time RT-PCR.  
**Molecular Cancer** 3, 5, 2004.
52. Widschwendter, M., Siegmund, K.D., Müller, H.M., Fiegl, H., Marth, C., Müller-Holzner, E., Jones, P.A., **Laird, P.W.**  
Association of Breast Cancer DNA Methylation Profiles with Hormone Receptor Status and Response to Tamoxifen.  
**Cancer Research** 64, 3807-3813, 2004.
53. Siegmund, K.D., **Laird, P.W.**, Laird-Offringa, I.A.  
A Comparison of Cluster Analysis Methods using DNA Methylation Data.  
**Bioinformatics** 20, 1896-1904, 2004.
54. Widschwendter, M., Jiang, G., Woods, C., Müller, H.M., Fiegl, H., Goebel, G., Marth, C., Müller-Holzner, E., Zeimet, A.G., **Laird, P.W.**, Ehrlich, M.  
DNA Hypomethylation and Ovarian Cancer Biology.  
**Cancer Research** 64, 4472-4480, 2004.
55. Kim, M., Trinh, B.N., Long, T.I., Oghamian, S., **Laird, P.W.**

Dnmt1 Deficiency Leads to Enhanced Microsatellite Instability in Mouse Embryonic Stem Cells.







**Nucleic Acids Research** 32, 5742–5749, 2004.

56. Theisen, J., Peters, J.H., Fein, M., Hughes, M., Hagen, J.A., Demeester, S.R., Demeester, T.R., **Laird, P.W.**  
The mutagenic potential of duodenoesophageal reflux.  
**Annals of Surgery** 241, 63-68, 2005.
57. Tsou, J.A., Shen, L.Y.C., Siegmund, K.D., Long, T.I., **Laird, P.W.**, Seneviratne, C.K., Koss, M.N., Pass, H.I., Hagen, J.A., Laird-Offringa, I.A.  
Distinct DNA Methylation Profiles in Malignant Mesothelioma, Lung Adenocarcinoma, and Non-tumor Lung.  
**Lung Cancer** 47, 193-204, 2005.
58. Cote, R.J., **Laird, P.W.**, Datar, R.H.  
Promoter hypermethylation: A new therapeutic target emerges in urothelial cancer.  
**Journal of Clinical Oncology** 23, 2879-2881, 2005.
59. **Laird, P.W.**  
Cancer Epigenetics  
**Human Molecular Genetics** 14, R65-R76, 2005.
60. Woodson, K., Weisenberger, D.J., Campan, M., **Laird, P.W.**, Tangrea, J., Johnson, L.L., Schatzkin, A., Lanza, E.  
Gene-specific methylation and subsequent risk of colorectal adenomas among participants of the polyp prevention trial.  
**Cancer Epidemiology Biomarkers and Prevention** 14, 1219-1223, 2005.
61. Sarter, B., Long, T.I., Tsong, W.H., Koh, W.P., Yu, M.C., **Laird P.W.**  
Sex differential in methylation patterns of selected genes in Singapore Chinese.  
**Human Genetics** 117, 402-403, 2005.
62. Weisenberger D.J., Campan M., Long T.I., Kim M., Woods C., Fiala E., Ehrlich M., **Laird P.W.**  
Analysis of repetitive element DNA methylation by MethyLight.  
**Nucleic Acids Research** 33, 6823-6836, 2005.
63. Fiegl H., Millinger S., Goebel G., Muller-Holzner E., Marth C., **Laird P.W.**, Widschwendter M.  
Breast Cancer DNA Methylation Profiles in Cancer Cells and Tumor Stroma: Association with HER-2/neu Status in Primary Breast Cancer.  
**Cancer Research** 66, 29-33, 2006.
64. Ogino S., Cantor M., Kawasaki T., Brahmandam M., Kirkner G., Weisenberger D.J., Campan M., **Laird P.W.**, Loda M., Fuchs C.S.

CpG island methylator phenotype (CIMP) of colorectal cancer is best characterized by quantitative DNA methylation analysis and prospective cohort studies.  
**Gut** In Press, 2006.

## BOOK CHAPTERS

1. **Laird, P.W.**  
DNA Methylation. (Chapter 24).  
In: Development: Genetics, Epigenetics and Environmental Regulation. V.E.A. Russo, D.J. Cove, L.G. Edgar, R. Jaenisch, F. Salamini (Eds.). Springer Verlag, Berlin, Germany, 1999.
2. **Laird, P.W.**  
Mouse Models in DNA Methylation Research.  
**Current Topics in Microbiology and Immunology**, 249, 119-134, 2000.
3. Huang, T.H.-M., Plass, C., Liang, G., and **Laird, P.W.**  
Epi Meets Genomics: Technologies for Finding and Reading the 5<sup>th</sup> Base. (Chapter 3).  
In: The Epigenome. S. Beck, A. Olek (Eds.). Wiley-VCH Verlag GmbH, Weinheim, Germany, pp 41-63, 2003.
4. Cottrell, S.E. and **Laird, P.W.**  
Sensitive Detection of DNA Methylation.  
**Annals New York Academy of Sciences**, 983, 120-130, 2003.
5. Sodik, N. and **Laird, P.W.**  
Mouse Models for the Study of DNA Methylation.  
In: DNA Methylation – Approaches, Methods and Applications. M. Esteller, Ed. CRC Press, Boca Raton, FL, 2004.
6. Campan, M., Weisenberg, D.J., and **Laird, P.W.**  
DNA methylation profiles of female steroid hormone-driven human malignancies.  
**Current Topics in Microbiology and Immunology**, In Press, 2006.

[PubMed](#)
[Nucleotide](#)
[Protein](#)
[Genome](#)
[Structure](#)
[PMC](#)
[Taxonomy](#)
[OMIM](#)
[Books](#)

Search  for

Limits  Preview/Index  History  Clipboard  Details

Display  Show

Range: from  to  ☐ Reverse complemented strand Features: ☐ SNP ☒ CDD

☐ 1: [AF027148](#). Reports *Homo sapiens* myog...[gi:3403164]

[Links](#)

[Comment](#) [Features](#) [Sequence](#)

LOCUS AF027148 12825 bp DNA linear PRI 07-AUG-1998  
 DEFINITION *Homo sapiens* myogenic determining factor 3 (MYOD1) gene, complete cds.  
 ACCESSION AF027148  
 VERSION AF027148.1 GI:3403164  
 KEYWORDS .  
 SOURCE *Homo sapiens* (human)  
 ORGANISM *Homo sapiens*  
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.  
 REFERENCE 1 (bases 1 to 12825)  
 AUTHORS Chen,B., Dias,P., Jenkins,J.J. III, Savell,V.H. and Parham,D.M.  
 TITLE Methylation alterations of the MyoD1 upstream region are predictive of subclassification of human rhabdomyosarcomas  
 JOURNAL Am. J. Pathol. 152 (4), 1071-1079 (1998)  
 PUBMED 9546368  
 REFERENCE 2 (bases 1 to 12825)  
 AUTHORS Chen,B.  
 TITLE Direct Submission  
 JOURNAL Submitted (26-SEP-1997) Pathology, University of Arkansas for Medical Sciences, 4301 West Markham St., Little Rock, AR 72205, USA  
 COMMENT Methylation alterations in the 5' region are found in embryonal rhabdomyosarcoma and alveolar rhabdomyosarcoma. Dynamic methylation changes in this region are found in normal myogenesis.  
 FEATURES  
 source Location/Qualifiers  
 1..12825  
 /organism="Homo sapiens"  
 /mol\_type="genomic DNA"  
 /db\_xref="taxon:9606"  
 /chromosome="11"  
 /map="11p15.4"  
 repeat\_region 1866..2513  
 /note="VNTR; polymorphic in the general population"  
 /rpt\_type=tandem  
 gene 8721..12783  
 /gene="MYOD1"  
 /note="expressed in early myogenesis and in rhabdomyosarcomas"  
 mRNA join(10264..11065,11555..11633,11908..12783)  
 /gene="MYOD1"  
 /product="myogenic determining factor 3"  
 CDS join(10436..11065,11555..11633,11908..12161)

```

/gene="MYOD1"
/note="Myf3; MyoD1"
/codon_start=1
/product="myogenic determining factor 3"
/protein_id="AAC29001.1"
/db_xref="GI:3403165"
/translation="MELLSPPLRDVDLTAPDGLCSFATTDDFYDDPCFDSPLRFFE
DLDPRLMHVGALLKPEEHSHPAAVHPAPGAREDEHVRAPSGHHQAGRCLLWACKACK
RKT'TNADRRKAATMRERRRLSKVNEAFETLKRCTSSNPQRLPKVEILRNAIRYIEGL
QALLRDQDAAPPAAAAFYAPGPLPPGRGGEHYSGSDASSPRSNCSGDMMDYSGPPS
GARRRNCYEGAYYNEAPSEPRPGKSAAVSSLDCLSSIVERISTESPAAPALLLADVPS
ESP'RRQEAAPSEGESSGDPTQSPDAAPQCPAGANPNPIYQVL"

```

## ORIGIN

```

1  ggatccagcg  tcagccacct  gaggaacatc  ccaacacatg  tcatgcctcc  gggccttcac
61  ccatgtctgtt  ctgtaagccc  ggaaagcctt  tctctacagc  agccccccga  cccacttttg
121  gcactcctat  tcatccttca  gtaaccaaga  agaaggatag  caatatttcc  tccttgggga
181  actcttcttg  ggtgtccaca  agagagttca  ttgttccctc  ttggtgctcc  cccaggggtg
241  tttgattatt  catttatgga  ttgctctttc  cccaacagac  agagctcttt  gaggctgggg
301  atgctgtctg  aatcatccct  agatcttact  gcacctaacc  tggggcctgg  aaacaggggt
361  ggtgtctggg  gaatgcttga  ggggttgggg  gaggttaggc  ctgttgaggc  gcatgggcca
421  taaatcacct  tcccaagcca  gggggaaagc  agcaatccag  gagagcttca  cggaggtggc
481  aggacgggat  gtaggacgga  ggcaaaccat  agactcgag  gcggtgaggg  catcattcat
541  gagacctctg  ccctccgttc  ttctgccagg  aaacccctgt  cctgggtgct  attggccagg
601  gataagcaga  ttttgagggg  gggaatcagg  cttcttcaag  gcgttaggtc  tccactcaga
661  ggtatgtggc  tggggcagct  gctgggggct  gcagctggtg  tctgtcccag  agcccaacgg
721  ctgtgtgtgc  cttaatccca  gtccttggtg  cccccaggc  tggcaggtgg  actgatgagg
781  cagaaaggag  gcaacaggag  aggggtggag  agccgagccc  cctctccagg  tccccacagc
841  cgccctctgg  atcttgctac  atgtgccacc  ccatcaccag  gtcctcgta  ccagctatcc
901  cctcagccct  gagctgctcc  tccctcagcc  cttagagggg  ggtctgacct  ccttgaggta
961  ggaagattca  gcttaaaaag  ttcaaactgg  aaaacacaaa  gaagagatgg  atgtcacggc
1021  atctgtgccc  cttagcgtct  tctttctgaa  tggggctggg  gatgtttagg  cacataggtg
1081  gagacaagca  ttcacactgg  gactgaggtg  tggacgtacc  taacttagaa  tatgagcagg
1141  tgggacgcat  ctgtggtgtg  cacatggcat  gtgaagtgtg  tgtgttctgt  aggtgagggg
1201  tgcacagcat  gggaggtata  cgcattgtgt  aggtgtgcat  ggactatgaa  gcatgcacag
1261  tatatgaggt  gtaatatgtg  tgatatgcac  atgatgtgag  agaggaaata  tcccatatgt
1321  gggacatact  gctgttgagg  gtttacatgg  catgtgagtt  tacatagagt  gtcaagtgtg
1381  tccggagtgt  taggtgtaca  tggcatgtaa  tgtgtaaaca  atgtgagact  tgtacatagt
1441  atgtgaggtg  acatggagtg  tgaggtgtgt  gtgtgtgtga  ggtgtacatg  gaggtagata
1501  tgtacacaat  ataagagatg  taccagtggt  gtaacatatt  catggagtgt  gaggtagaca
1561  tggcacaaga  gagatacaca  cagtgcctga  gatatatgtg  gtatgtgagg  tgtacagaga
1621  ggggtgaactg  tacattatgt  gagaggtgtg  cagtatgtga  gaggtgtaca  gtatgtgaaa
1681  ggtgtgcagt  atgtgaaaga  tgcacattat  gagagaggtg  gatggagcat  aaggtgtaca
1741  ttatgtgaca  ggcatagagg  gaacgtgagc  tttacattct  gtgagaggca  cataggaatt
1801  gtgaggtgta  cactatgtga  gaggtataca  ttatgtgaaa  gatgtacatt  atgagagaag
1861  ctgcaggcag  catgtggtgt  acatcctgtg  agaggcgtgc  agggagtgtg  aggcgtgctg
1921  tctgtgagag  gcatgcaggg  agtgtgaggt  gtgtattctg  tgagaggcgt  gcagggggtg
1981  tgcggcgtgc  attctgtgag  aggcattcgt  ggagtgtgca  gcatgcattc  tgtgagaagc
2041  gtgcaggagg  tgtgaggcgt  gcattctgtg  agaggcgtgc  agggaatgtg  aggcgtgcat
2101  tctgtgagag  gcgtgcaggg  agtgtgaggg  gtgtattctg  tgagaggcct  gcagggaatg
2161  tgaggcgtgt  attctgtgag  aggcgtgcag  ggagtgtgag  gtgtgcattc  tgtgagaggc
2221  gtgcagggaa  tgtgaggcgt  gtattctgtg  agagggtgtg  agggagtgtg  aggcgtgcat
2281  tctgtgagag  gcgtgcaggg  aatgtgaggg  gtgtattctg  tgagaggtgt  gcagggagtg
2341  tgaggcatgc  attctgtgag  aggcattcgt  ggagtatgtg  gcatgcattc  tgtgagaggc
2401  gtgcaggggg  tgtgtggtgt  gcattctgtg  agagggtgtg  agggagtgtg  aggtgtacat
2461  tatcagagag  gtgtacaggg  agcgtgcact  gtatatgtgt  tgagaggtgt  gcacagtgtg
2521  aggtgagcac  tgtatgtgac  ttgtctgcag  tttatcaggt  gcacatagct  atgacaccac
2581  aaaggcatat  ggaagaatgc  aggtgaggac  aaactgtcct  tccaagaaaa  tgtgcttgtc
2641  agctctgtcc  tgggctcaca  ctctggacgc  atggcacaac  ctctgagca  gtgtcacagg
2701  cagaggagac  agagggacgt  cctctggcct  ttcaggagtc  cttttatata  taaaggagaa
2761  ggcagctttg  agaggccttc  tcctccatcc  ttctgcctgc  atccatacca  cgtagctca

```

```
2821 agggcaatgt gctctttgag gaataccata cgttggtaat attattttta catctgactt
2881 aaatccctca tgctgcaagt tgaattcgca tttttttggt gctttcaaat gtgaaggtag
2941 tgaactctcc tttcatgtag acctcctcac cccgggagcc taatgtcttt aggctagaag
3001 aataattagc accttcatga gctctgcctg cttgaacact tctagtcatt aagttattgt
3061 caccttattt gtgttgttta gtaaacagcg catgtgtatt tcaaacccca ggaatctagt
3121 cccacaaaga ccccagggtc cacctctgag gcagagaaag tctttaatta cataaagaat
3181 aagcttgaag aagagagggt ggtatgaatga atgaacgcct cagggtcttc cagaagccag
3241 gcatcagtgg gttcttaagc ctggcctcag cttccctac ctgggtgggca gtctcagctc
3301 ctgctatttt cactcatctg gcttcctagt gtctgggaaa gaaccggag tgagaggcat
3361 tgtgagggtc gcatggaatg tgagggtgcac atggcatgtg gggcctcgtg ggggaaagag
3421 ctgggcgggc tgcaggagg gtcccccat aacaccaagc tcacatgggt cacatcccat
3481 gcccttttagc ctcttccctt gggtagcagc ccacctcat ctcacatcct gaattgggct
3541 aaagcttagt tctagatgaa gttataatta aattttaaata cacatctaga gaattccctc
3601 ttaaatttaa gtactatgtc agttttggag ggagttttta taaacctatt gaagagggga
3661 ataaacagct ctagcctatt atgcctagtt cttcaagaat ctcttggttt gtaagatatt
3721 ctttcattag aagtaacaaa ttggccagggt gcgggtgggt catgcctgta atcccagcac
3781 tttgggagc tgaggcagggt agatcacctg aggtcaggaa ttcgagaaca gcctggccaa
3841 catggtgaaa ccccatctct actaaaaaca cacaaaaaat agccagacat ggtggctcgc
3901 gcctgttgtc ccagctactc aggaggctga ggcacgagaa tcgcttgaac cccggcagca
3961 aaggttgtag tgagctgaga tcgcgccact gcactccagc ctgggcgaca gagcgagatt
4021 ctgtttcaat tttttaaaaa agaagaagaa gtaacagatt gcccatcaaa ccccatgccc
4081 aaactctatc tcgtgccacc cccacacccc ccagccccta cagctccagg agccatgcct
4141 gtctgtaccc acagaaatcc tctgtccta gcagaagcga ttgtcccata gaaggtgctc
4201 aataattatt ttgttctctc tgccgggagc attcttcccc agatgccaca tggctaactc
4261 ccaagcctct ttttaactct tgctcaaatg ttaccttgcc aacctgacca ctctgtttaa
4321 cactacagcc gacccaacc tggcacctca atcctgctca tcttgttctg cttgtaatat
4381 ttttctgcgt gtatcgctt ctaacctcta tataatttat ttattattat gtgtattgct
4441 tattgtctgc cctgccctgc ccgcatgtca gttccacagg aacaaggaac atgggtctgtt
4501 tcattctcca tcacattccc agcacctgaa taaatgtttg ttgtataagt gaatgaatca
4561 tagactggac aactgagagt gggaaatatc ccaccacccc aatagtgcc tgccccacc
4621 ccctgcacac tgggtgggaa gggcacatgc tgttggttgt cttcctgttc cctccctcca
4681 cagtgtggac tcctgttctt caactccag ctgagctgcc agactcctaa gccctgcttg
4741 tctgtgggag gctggagagt acccccaaag ggggaaatgt ggccttctgt gaggaatctc
4801 tgggaccctg tcctaattct gggaccatgt ctatatcctg gcaatatcac agtccctcct
4861 gaccaacca gactgggccc agagaaggat ctatacccat gtggtgggtg gattttggct
4921 ttcccaggga gcaagtttgt caggggacag agggaggcac tcaggttgga cccaggaaca
4981 ggaagggaaa ggctggggac agagagggga cctggagctg gccctgcccc accaggccca
5041 ctcatgcttt taccttctgg ccctttggcg ccccccactt cccggccaga tacgcagcct
5101 gtgtcagccc cagtgcagag ccacaggccc agcttgggca ggggcagggt gcgtgaagac
5161 tggggcagggt gcaggctgga ttgggtttcc agaggctata tatataaagg ctgccgggag
5221 ccccagggcc gctccctgag ggcacaacac tgtgggggcc cagccaggcc cgcattcctt
5281 tccagaggcc agctttccat ttatagcccc tgggcagagc agccaaggga gctgagaggg
5341 gaggactgga aagggcagag ggagaagggg cagcccaggc agcactccct ccccatccc
5401 caccaaagta gccctcatc atgaagacag cagaagccag gccaggggc aggtgtgcac
5461 atgcccccaa gcacagagcc taccattctg gtcagacctg cgttgagggg tgagggggct
5521 gccagggatc cctcaaagtc ctcagcccat tgctagtggc ccctcacaga acaagtccag
5581 cacctgtgga caaagggcac ccttgactag actctgcagt ataagagttt gaatgttttc
5641 agcttccaaa cttggtatcc tttttccctc cgccccaac ccagcactgg gactaaaagg
5701 acaacatgtc ccaggttgga catacttctc cctgctctgt gggcagcagg gaagagatga
5761 tgggtgttgac aaacctctct ccaaagagga gacgcaacca gaagggtgat tccaggcagg
5821 tgtggatgcc aggcattggag aggtctgaaa tggtcaccga gttcagttag ttccaatctt
5881 tttttgagca acggaagcct ggtagcaaac aaaaatccca cttgaaagcc taatataaaa
5941 atggcatttt acccctagaa tgtctgtgtg ctttaaaaca gcgcttccta attatgggaa
6001 gaagatgtag ctgcaaatca agcttaaaac tgtcaaagca gtttagattt ataagccata
6061 agtgataaaa tattaatgt gtttggttaag ttcaaacata taacatttac ttatttattg
6121 taaaggcaac ttgatgacag ccctgaggaa gtttttagaa actcaaagca caaaaagcaa
6181 agttgtatcc acttgtctca gcatccaatt tattttgtag tttcttgctt attcagattt
6241 ggggaaaatc tagatttgca tagataagtg gtttgaatag ctcacctggg aatctcagag
6301 tactctttta ttaagtagac tcattcattc atttgcccaa gaaatattta ttgagtgcct
6361 actatgcacc tggctttctg ctgagcctga gcaagtagga agagtatttg tttctaaatc
```

```
6421 atcaatacaa caattactta cattcctcat tgtgagtata gtgaaaaaac aataagaaga
6481 cacatcgaga tgccaaatct ctctatagta taccactaca atattgcagc atgccatgta
6541 taatgcccag ttcaagagaa catgccccag gcagatgggg tctgagcctt tcctgggaag
6601 agcaagtgtg atagaacatg gatgtctaat catgtatgtg acttcccagt tttgaagaaa
6661 ttcaaccatc ttcattaatg tcacagttca agacgttcaa atatatgcat agagatgcaa
6721 agggcgtgag gccactcatt cattcactgg acatttatca ggtgcctact gtgtgactgc
6781 cactgtgatg gtttttggaa atgtcattgt gaacaaaaca tctttgcctt catggggcta
6841 agtcagtcac gaacaaacta atgaagaaga ttataaagag tggcagtgcc tgggaaggaaa
6901 ttaacagggg ggtgtgaacc agagtatggg gggcagttat cttagagggg atggtcagtg
6961 atgtcccaag gaggcaagaa gatctattat ataaaatgca gtcaatcttg ggaaaagccc
7021 aggggataat gctatgagtt tagagcagca aggacaaggc tccaaggcag gatcctgttc
7081 agagtgttag aagacaagaa aggaggtcag gctaactgga gtagagcaat caaaacggat
7141 ggtgcctcca ggtgtagtaa gagacacagg ctgaggctag ctcatgcagg gcctgatagg
7201 ccaggggatg gagatgagat tttactctaa atgcaagaag ctgctgggga gtttgaagca
7261 ggaggatggc ataatcccat ttacattgta aaggtctact caggctgcta tgtaacgaat
7321 ggattatact gaggtacag aggaagttag gagggcagcc aggttattgt ggtcatccag
7381 agcagcagtg tgacagctta gtccaggatg gtgacactag ggatggactg acttgagaca
7441 ggtcttagag gtagaatgga cagctcttcc tcatactcag acctctcctt gggaaactcca
7501 gccttaaaaa tccccctgcc taatccacac ttccatctgg atatccgata tgcatttcaa
7561 atttttgccc aaacctggac acttaatcta ccaccacaa acctagtctt ctcaactcca
7621 ttcttgccag agtcacacct agctccttgc ttatctcact tcccacatgc aatcgtgagt
7681 aaatactgct agctccatct tgaaaacata tatctagaat tcaaccacca cttttcacca
7741 gctccactca ctggggatta ttgcaatagc ctctaattg gtctccctcc ttctgcctt
7801 tccctccagt aaccagcatg ctctgttaa aatgtaaatc agatagtgat attcttctct
7861 tccgctcaag cctccagtg agatggctca agccatctca gaatataatc ctgtttctct
7921 ctctctcacc ccatttccca ctatctcttt tactaccct gctgcagaca tatgaccctc
7981 cttgccatac tttgaatctg ccaaacatgg tcctgcctca ggacttttgc acatgcttat
8041 ccctctatct ggccctacat atctccagggt atctgcttcc aattctcttc attcagggtc
8101 ctgcttaaat gtagcagaga ggcttctct aatcactcca taatcttcat cactgtgtct
8161 ccctgccttg ctttttcttc ataaggcttc taacctctg gcacacata cttccttgct
8221 tatttgttca ttgtctatca ccctgcttac attgacaatg taagtgccat gtaagcagag
8281 tcttggtttt gttcattgct ctagccccac acttggtact gtacctgcca cataatggat
8341 acctaaacat atgtggattt ccgggtgacc cctgcagctt ggggtggggtg aggcagaact
8401 tgctggctct gccaggattt agagttactg tcaactgctg tccatgatgt agactttact
8461 gaatgaacaa atacaggtgg gccctatgga gtaaagcgag gtgagtactt catgaaggga
8521 gaccttcagc accactacca gcagcagaga agtgaagaag ttaggacccc aacagagccc
8581 tctgagtttt gtgggaaggg aggacttctt agggcccaga acggccagct agaatgcctt
8641 ccagaagtta gtgggaagg cacaagatc actcctgctt aaatttcttg tttccaggag
8701 gggagatcca ggcagggatg tatggccaac ggagattcct agccagagtg ctgagaggac
8761 tgtgtgaact gcagattcag gaagaggctg agagaccccc atgggggttg ccggtatgct
8821 gaggcttgta tgggagccag atatcccaca tcccatgggg tggttgcctc ctctgtttc
8881 cagcctttcc agtgaggctg caggaaagag acacagctaa ggcttgaga ctcgtggcac
8941 tccgtcaggg catggtacca cagatgagtt gtaagcctgc gggacacagc atccaactct
9001 gaaagccctt tgctcgaata accctacatc accgcctgag ggcttccata tccttggtct
9061 cttcagactg tcatccccac cacaattact ccaagaaatt actgtcatcc ccaaacttat
9121 aactggaaac tgaggctcag gaaggagaca tgacttccac aaaatcacac agttgggaaa
9181 ctctggagtc tgcactcaac tggcttgcaa accgactctc ggagacttca ggtgagatga
9241 ggtcaggttc tcaggccagg tcctgaagtt tgacaccttg gcgaaatgca ctttcttga
9301 ctcagcaccg cagtgcaggc ggaacgaagc cccgagcaga agggcttttc tcccagctg
9361 aagaggcagc tcagcctaga cccaggcat ggcactggac acccctgctg tggaaacgtg
9421 cagattttaga tggaggggat tcctaacctg ggcaggatcc gagtttgag agattggcgc
9481 gaagtttagc agcaatctcc gattcctgta caaccatagc tgggtttcta agcgtctagg
9541 gaagaaggac tgggcccacg acctgctgag caactcccag gtcggggact ggcggaatat
9601 cagagcctct acgaccctt tgtctcgggc tcgcccactt caactctcgg ggtctctccg
9661 cctgttggtg cactcgtgcg ttctctgccc ctgacgctct aagctttctg ctttctgcgt
9721 gtctctcagc ctctttcggt ccctctttca cggctcact cctcagctct gtgccccaa
9781 tgcttgctt ctctccaaat ctctcacgac ctgatttcta cagccgctct acccatgggt
9841 cccccacaaa tcaggggtac agaggagtat tgaaagttag ctgagagggt agcgcgcgca
9901 gccagcgttt cccgcggata cagcagtcgg gtgttggaag ggtttggaag gggcgtgccg
9961 gagagccaag tgtcagccgc ctagggtctg ccggtcgctc cctccctccc tgcccggtag
```

```
10021 gggacctagc ggcacgcca gtgtggaggg ggggctggc tggccagtct cgggcccctc
10081 gggcaccccg gggaccccc ccaagcccc ccccgagtg ttctattgg cctcggactc
10141 cccctcccc agctgcccc ctgggctccg gggcgtttag gctactacgg ataaatagcc
10201 cagggcgctt ggccgagaag ctaggggtga ggaagccctg gggcgctgcc gccgctttcc
10261 ttaaccacaa atcaggccgg acaggagagg gaggggtggg ggacagtggg tggggattca
10321 gactgccagc actttgctat ctacagccgg ggctcccag cggcagaaag ttccggccac
10381 tctctgccgc ttgggttggg cgaaagccag gaccgtgccg cgccaccgcc aggatattga
10441 gctactgtcg ccaccgctcc tgcacgtaga cctgacggcc cccgacggct ctctctgctc
10501 ctttgccaca acggacgact tctatgacga cccgtgtttc gactccccgg acctgcgctt
10561 cttcgaagac ctggaccgcg gcctgatgca cgtgggcgcg ctctgaaac ccgaagagca
10621 ctcgacttcc cccgcggcgg tgcaccggc cccgggcgca cgtgaggacg agcatgtgcg
10681 cgcgcccagc gggcaccacc aggcgggccc ctgcctactg tgggcctgca aggcgtgcaa
10741 gcgcaagacc accaacgcgg accgccgcaa ggccgccacc atgcgcgagc ggcgccgctt
10801 gagcaaagta aatgaggcct ttgagacact caagcgtgc acgtcgagca atccaaacca
10861 gcggttgccc aaggtggaga tctgcgcaa cgccatccgc tatatcgagg gcctgcaggc
10921 tctgtgcgcg gaccaggacg ccgcgcccc tggcgccgca gccgccttct atgcgccggg
10981 cccgctgccc ccgggcccgc gcggcgagca ctacagcggc gactccgacg cgtccagccc
11041 gcgctccaac tgctccgacg gcatggtaag gccgggaccc caggaagtga ggaagttagg
11101 gcggcgctcg ggatatcagg gacgcgtttc cgagggcggg gagctggcct tgcgggaggt
11161 ttgggcccagg atccttccc agagagagga ccccttgtc ctgggcagct gtcactgggg
11221 tagcctgttt tggaaagtgt cgggcaagcg ttcgagctgc ccatttgggg gcgctattag
11281 aacactgcag cgcgaacgtg aagatctttt tctctactta tccctacttc caaaatgtaa
11341 atttgcgccc cttggtgact gtccgccctt ggtttggccc tgcattgtgc agacctcatc
11401 tcctaccac ccgtaattac cccccaacc aggacaggtc tgggcccga actagagcct
11461 taggctagag ttagggaggg ggcggctaca ggaattggtg ttcgggcctc gagcgtccc
11521 gcgggcctga ctcagtcgcc cttgctgttt gcagatggac tacagcggc ccccgagcgg
11581 cgcccgcgcg cggaactgct acgaaggcgc ctactacaac gaggcgccc gcggtgggta
11641 ttccgggcct cccctgctc gtcctcctc cttcatggag ctgtcctggc ctctatctag
11701 gacgtccca ccccaactca cacacgccta tgtcctggga agtgggtgcg gagatgaaat
11761 actaagcaag tagctccctg tcttttcgat tgtcccgac tctaactaaa gtccctcagtt
11821 tccaatctgt ctcaaagtac tgggcccggg ggtgggaggc ttgtcgcggc cccacccttg
11881 cttactaacc gagccctccc cgcgcagAAC ccaggcccgg gaagagtgcg gcggtgtcga
11941 gcctagactg cctgtccagc atcgtggagc gcattctccac cgagagccct gcggcgcccg
12001 ccctcctgct ggcggacgtg cttcttgagt cgcctccgcg caggcaagag gctgccgccc
12061 ccagcgaggg agagagcagc ggcgacccca cccagtcacc ggacgcgcgc ccgcagtgcc
12121 ctgcgggtgc gaacccaac ccgatatacc aggtgctctg aggggatggg ggcgcccac
12181 ccgcccagg gatggtgccc ctagggtccc tcgcgcccAA aagattgaac ttaaagccc
12241 ccctcccaac agcgctttaa aagcgacttc tcttgaggta ggagaggcgg gagaactgaa
12301 gtttccgccc ccgcccaca gggcaaggac acagcgcggt tttttccacg cagcaccctt
12361 ctcgagagac cattgcgatg gccgctccgt gttcctcggg gggccagagc tgaaccttga
12421 ggggctaggt tcagctttct cgcgccctcc cccatggggg tgagaccctc gcagacctaa
12481 ccctgccccg ggatgcaccg gttatttggg gggcgctgag acccagtga ctccggtccc
12541 aaatgtagca ggtgtaaccg taaccacccc ccaaccggtt tcccggttca ggaccattt
12601 ttgtaatact tttgtaactt attcctgtaa ataagagttg ctttgccaga gcaggagccc
12661 ctggggctgt atttatctct gaggcatggg gtgtggtgct acagggaatt tgtacgttta
12721 taccgcaggc gggcgagccg cggcgctcg ctcaggtgat caaaataaag gcgctaattt
12781 ataccgcggt ggctccggct ttccctggac atgggtgtgg gatcc
```

//

[Disclaimer](#) | [Write to the Help Desk](#)  
[NCBI](#) | [NLM](#) | [NIH](#)

Feb 1 2006 13:21:03